CADTH Health Technology Assessment

Opioid Analgesics to Treat Chronic Noncancer Pain Among Patients Prescribed Opioid Agonist Therapy or With Opioid Use Disorder

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Protocol

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Abbreviations

AMED	Allied and Complementary Medicine Database
CI	confidence interval
OAT	opioid agonist therapy
OR	odds ratio
OUD	opioid use disorder
RCT	randomized controlled trial

Introduction and Rationale

Opioid use disorder (OUD) is a chronic and relapsing pattern of opioid use associated with significant impairment. It may occur in the context of prescription opioid use (i.e., for analgesia), street opioid use, or the combination of both.[1,2] OUD is a growing public health concern across North America and disproportionately impacts some social groups.[3]

In Canada, the prevalence of OUD varies across jurisdictions, with the estimated prevalence in British Columbia (1.92%) being 2 times the nationwide prevalence.[3,4] Likewise, rates of opioid-related harms vary nationally, with fatalities and hospitalization rates being highest in Canada's western jurisdictions.[5] OUD and opioid-related harms remain serious issues across the country, with opioid overdoses among the leading causes of death in adults.[3] The national rate of apparent opioid toxicity deaths in 2022 was estimated to be approximately 19 per 100,000 population[5] and harms have accelerated during the COVID-19 pandemic; for example, in Ontario, opioid-related life-threatening emergency department visits increased by 57% and opioid-related deaths increased by 60%.[6,7]

Chronic Noncancer Pain and OUD Comorbidity

Chronic pain, defined as pain lasting 3 months or longer, is also a major clinical and public health issue, with about 1 in 5 people in Canada (nearly 8 million people) living with chronic pain.[8] People with OUD are more likely to live with chronic pain, as indicated by a systematic review that reported rates as high as 45%.[9] Upwards of 8% of individuals with chronic pain are estimated to have a history of OUD.[10]

There is a complex interplay between these 2 conditions. Chronic pain may precede or follow a diagnosis of OUD[11,12] as prolonged use of opioid analgesics for the management of chronic pain can increase the risk of developing OUD, while people with a history of OUD who also have chronic pain may use opioid analgesics that exacerbate their addiction.[13] People with chronic pain often take opioid analgesics for pain management, and with regular use will develop physical dependence to these medications. In 2018, 12.7% of people living in Canada (approximately 3.7 million) aged ≥ 15 years reported using opioids for pain relief over the past 12 months; of these, 9.7% (approximately 351,000) engaged in problematic use (defined in the study as taking opioids in greater amounts or more often than directed, intentionally using them for the experience or to get high, using opioids meant for pain management for reasons other than pain relief, and tampering with a product before taking it).[14]

The co-occurrence of chronic pain and OUD is associated with a 55% increased likelihood of overdose relative to those with OUD and without chronic pain (odds ratio (OR) = 1.55, 95% CI: 1.16 to 2.08).[15] Furthermore, increased severity of chronic pain in individuals with OUD is associated with worse health-related quality of life.[15] While chronic pain is already routinely linked to poor psychosocial functioning, reduced quality of life, and poor self-rated health, the impacts of chronic pain are likely worse in individuals with OUD.[17]

The majority of people with OUD also have at least 1 coexisting psychiatric disorder.[11,16,17,18] This is of heightened concern among individuals with co-occurring OUD and chronic pain: a meta-analysis showed that the likelihood of psychiatric comorbidity in individuals with OUD was more than 2 times as high in those with co-occurring chronic pain than in those without chronic pain (OR = 2.18; 95% confidence interval [CI],1.6 to 2.9).[19] Other studies have similarly suggested that the prevalence of mental health concerns is significantly higher in people with OUD that have chronic pain (67% to 78%) than in those without chronic pain (51% to 58%).[13,20]

Given the high rates and complexities of this comorbidity, effective guidance for the management of chronic pain is critical for improving the care of people with OUD.[11]

Available Treatment for Co-Occurring OUD and Chronic Pain and Challenges

Managing chronic pain in individuals with OUD presents unique challenges.[11] In many jurisdictions, opioid agonist therapy (OAT), commonly using methadone, buprenorphine, and/or slow-release oral morphine,[2,10,21,22] is considered a first-line therapy for OUD. However, OAT alone may be insufficient to effectively manage chronic pain in people with OUD;[10] for example, though buprenorphine formulations are widely used for analgesic purposes, buprenorphine has been found to provide limited analgesic effect in individuals with co-occurring OUD and chronic pain.[23]

Clinical practice guidelines for the management of OUD[2,24–28] frequently include recommendations for treating chronic pain in patients with OUD, though the evidence supporting these guidance statements for chronic pain management is limited. Most guidelines recommend that patients with co-occurring OUD and chronic pain should be supported in exploring alternative pain treatments, such as nonopioid pharmacotherapies (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], anticonvulsants, and tricyclic antidepressants)[2,24,26] and nonpharmacological therapies (e.g., cognitive behavioural therapy),[2,25,26] that are accessible and culturally appropriate.

Evidence supporting the use of cognitive behavioural therapy[29,30] and mindfulness-oriented recovery[31] for treating chronic pain in patients with OUD is growing, but further studies are needed to establish their effectiveness in this context. Likewise, many medical professionals prescribe nonopioid medications for chronic pain; however, despite some positive findings, the analgesic effects of nonopioid medications for people with OUD are modest at best.[32]

These therapeutic limitations highlight the need to consider appropriate analgesic options in this comorbid context. One algorithm for managing chronic pain in patients with substance use disorders recommends using opioid analgesics when patients do not adequately benefit from other treatments, namely agonist therapy, nonpharmacological pain treatment, and psychiatric and/or sleep disturbance treatments.[33] Of note, with regards to efficacy, a meta-analysis found that opioid use among patients with chronic noncancer pain was associated with statistically significant, but clinically modest,

improvements in pain, sleep, and physical functioning; however, patients with comorbid OUD were typically excluded from these trials.[34]

Not all patients are the same, nor will they experience treatments the same. Rather, decision-making around therapeutic trials are informed by patient values and preferences, costs, accessibility, and other concerns.[35] While the risks and adverse effects related to opioids are significant, some individuals may still prefer them if they feel their pain relief benefits outweigh the side effects and concerns.[36]

Opioid analgesics are 1 option for chronic pain in patients with OUD. As it stands, however, guidance on the use of opioid analgesics to manage pain in this population is limited.[19] As concerns around poorly treated pain, opioid-related harms, health service utilization, accessibility, and costs grow, developing evidence-informed strategies for managing chronic pain in individuals with OUD and/or a history of OAT is critical.[11] Making relevant evidence readily available to patients, clinicians, health administrators, and policy-makers through evidence synthesis can support evidence-informed decision-making in this complex area. Accordingly, this project aims to summarize evidence on the efficacy, effectiveness, and safety of opioid analgesics in managing chronic pain in patients with OUD, a history of OUD, receiving OAT, and/or a history of receiving OAT.

Project Scope and Protocol Development

The methodology employed for this review follows the guidelines outlined in the Cochrane Handbook.[37] Reporting of the protocol adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Protocols (PRISMA-P).[38] Following the scoping and refinement process, the group finalized the research and policy questions and selection criteria with jurisdictional input.

The protocol was developed by the Subject Matter Health Research Lab based out of Humber River Health, in collaboration with CADTH and content and methodological experts (refer to Appendix 2). The protocol will be posted on the CADTH website for stakeholder feedback. This protocol has been submitted for registration in PROSPERO (international prospective register of systematic review). The evidence syntheses will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 reporting guidelines.[39]

Objectives

The main objective of this evidence synthesis is to explore the safety, efficacy, and effectiveness of opioid analgesics for the management of chronic pain for people with OUD, with a history of OUD, who are currently receiving OAT, and/or were previously receiving OAT.

Deliverables

The following deliverables are planned:

- a Protocol
- a Science Report
- a Summary and visual tool to aid knowledge dissemination.

Policy Questions

1. How can opioid analgesics be used safely and effectively in patients with chronic pain who are currently, or were previously, receiving OAT?
2. How can opioid analgesics be used safely and effectively in patients with chronic pain who are not receiving OAT and have an OUD or a history of OUD?
3. Are patients with chronic pain who are currently, or were previously, receiving OAT at a higher risk of overdose or relapse? Is there a duration of sustained remission from OUD where the patient is at minimal risk of relapse?

Research Questions

The project will address the following research questions. Details on the specific interventions and outcomes are included in Table 1.

1. In people with chronic pain who have OUD, a history of OUD, and/or are currently receiving OAT or were previously treated with OAT, what is the efficacy and effectiveness of opioid analgesics versus any direct comparators with respect to pain intensity, health-related quality of life, physical functioning, emotional functioning (anxiety, depression), and global rating of improvement?
2. In people with chronic pain who have OUD, a history of OUD, and/or are currently receiving OAT or were previously treated with OAT, what is the safety of opioid analgesics versus nonopioid therapy with respect to relapse, misuse, abuse, diversion, overdose, hospitalization, and death?

Table 1: Selection Criteria

Criteria	Description
Populations	Adults receiving OAT or previously treated with OAT who require treatment for chronic noncancer pain Adults with chronic noncancer pain who are not receiving OAT but have a diagnosis of OUD or a history of OUD
Intervention	Opioid analgesics

Criteria	Description
Comparators	Any comparator, including no treatment
Outcomes	Any 1 of, or combination of, the following: • Efficacy and effectiveness: pain intensity, HRQoL, physical functioning, emotional functioning (e.g., anxiety and depression), and global rating of improvement[40] • Safety: relapse, misuse, abuse, diversion, overdose, hospitalization, death
Study designs	Randomized controlled trial, clinical practice guidelines, systematic reviews, open-label treatment studies, observational (prospective or retrospective) studies, including cohort, case-control, and cross-sectional studies. The primary research studies informing clinical practice guidelines will also be used.

HRQoL = health-related quality of life; OAT = opioid agonist therapy; OUD = opioid use disorder.

Clinical Review Methods

Literature Search Methods

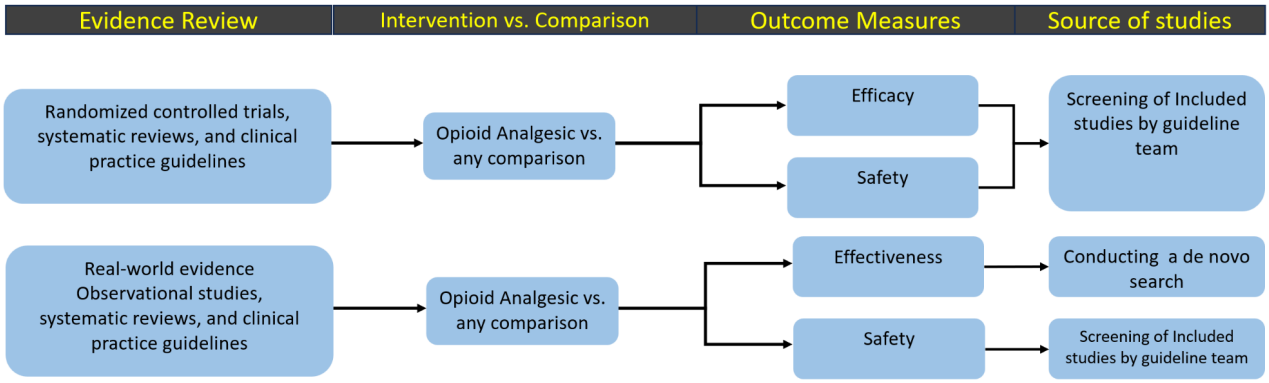
This evidence synthesis will focus on 2 kinds of outcomes (i.e., efficacy or effectiveness, and safety) informed by 2 bodies of evidence, namely randomized controlled trials (RCTs) and real-world evidence in the form of well-designed observational studies. As such, this synthesis will be informed by 4 subreviews focusing on: efficacy using RCT data, safety using RCT data, effectiveness using observational study data, and safety using observational study data (refer to Figure 1).

RCTs provide more robust evidence for establishing cause and effect relationships between interventions and outcomes due to their rigorous design and aspirations to control for confounding factors. However, observational studies are valuable for studying real-world scenarios and assessing associations between variables that might be difficult or unethical to study through RCTs.[41,42]

Observational studies may provide better representativeness for the target questions; RCTs often exclude patients with prior or current OUD, which can limit their applicability to real-world situations. Furthermore, observational studies are more appropriate for studying long-term and infrequent or rare harms. RCTs are typically small in scale and follow participants for fewer than 6 months, making it difficult to capture and assess long-term effects and rare adverse events.[43]

Both types of studies contribute to the body of evidence in health research, and researchers, clinicians, and policy-makers often use a combination of both to draw more comprehensive conclusions and inform practice and policy.[41,42]

Figure 1: Summary of Evidence Reviews and Source of Studies



vs. = versus.

RCT Data — Efficacy and Safety

Efficacy and safety of opioid analgesics for treating chronic pain in individuals with OUD or a history of OUD, or who are receiving OAT and/or were previously treated with OAT will be assessed using data from RCTs. The *2017 Canadian Opioid Prescribing Guideline*[44] was endorsed by a systematic review and meta-analysis that explored the efficacy and safety of opioid analgesics for treating chronic pain.[34] The authors included RCTs that explored the efficacy and safety of opioid analgesics versus any nonopioid analgesics. The review reported several outcomes, including pain relief, quality of life subscores, quality of sleep, and adverse events caused by opioids.

In preparation for the 2023 update, the evidence synthesis team for the guideline has updated a search for RCTs on MEDLINE, EMBASE, PsycINFO, CINAHL, the Allied and Complementary Medicine Database (AMED), and Cochrane Central from inception to July 2023. They have also reviewed the reference list of all included studies and relevant reviews.[45] For this project, the included studies from this update will be screened against the inclusion criteria for this project to specifically identify RCTs that have examined efficacy and safety within the context of OUD and OAT.

Real-World Evidence From Observational Studies — Effectiveness

For this body of evidence, an experienced medical librarian will design the search strategy by using controlled vocabulary and keywords representing the concepts “opioid,” “chronic pain,” and “opioid use disorder” (refer to Appendix 1). The evidence synthesis team will adapt the search strategy and conduct systematic literature searches in MEDLINE, EMBASE, PsycINFO, CINAHL, and AMED from inception to September 2023 without language restrictions. The evidence synthesis team will use the CADTH search filters for study designs to limit our search to observational studies, systematic reviews with or without meta-analyses, and guidelines in order to identify real-world evidence for the effectiveness of opioid

analgesics in treating patients with chronic pain who have OUD or a history of OUD, and/or are receiving OAT or have previously received OAT. After getting feedback from stakeholders, the search strategy will be reviewed following the Peer Review of Electronic Search (PRESS) guidance.[46]

Real-World Evidence From Observational Studies — Safety

The study team responsible for updating the *2017 Canadian Opioid Prescribing Guideline* has conducted 2 systematic reviews and meta-analyses exploring predictors of fatal and nonfatal overdose and OUD following prescription of opioid analgesics for chronic pain. Those reviews used observational studies to evaluate the risk factors associated with opioid overdose, opioid addiction, and death from opioid use, as well as OUD following the prescription of opioid analgesics for treating chronic pain. For both reviews, a health sciences librarian developed a search strategy and systematically searched MEDLINE, EMBASE, CINAHL, PsycINFO, and AMED from inception to July 2023. The evidence synthesis team will review the bibliographic references of the included studies and related reviews for additional potentially eligible citations. The evidence synthesis team will screen eligible studies from these reviews and include articles that enrolled patients with chronic pain who had OUD or those with a history of OUD and/or receiving OAT or previously treated with OAT, or explored these factors for their association with the relevant outcomes.

Updates

For all data sources, including RCTs and observational studies, alerts will occur until the draft report is in the publishing phase; however, the primary study results will be incorporated into the results section until the start of the stakeholder feedback and external review phase. Any relevant studies identified after this point will be described and referenced in the Summary of Results section.

Selection and Eligibility Criteria

Study Selection

For records obtained from the Canadian opioid guideline team, 2 reviewers will independently assess eligibility based on the predetermined selection criteria using the full text of the studies (refer to Table 1). This will be done using the web-based systematic review software Covidence, which was developed by Veritas Health Innovation in Melbourne, Australia, as 3 separate reviews to facilitate appropriate tracking of records and selections.

For the novel search for observational effectiveness data, pairs of reviewers will use Covidence and a standardized form to independently screen the titles and abstracts identified through our literature searches for relevance to the clinical research question. Before the formal screening process, we will perform multiple rounds of screening to achieve agreement. For each round, 50 titles and abstracts and 10 full texts will be used for pilot screening. Pairs from the same set of reviewers will independently

assess the full texts of all potentially eligible articles based on the predetermined selection criteria (refer to Table 1).

All conflicts will be resolved through discussion to reach consensus, and if needed, a senior reviewer will be involved. The study selection process will be presented in a PRISMA flow chart.

Inclusion and Exclusion Criteria

The evidence synthesis team will include RCTs of any design and observational studies, inclusive of both comparative and 1-arm observational studies that enrol at least 20 participants in their cohort. The team will include studies that enrolled adults with chronic pain (defined as pain lasting ≥ 3 months) who have OUD, have a history of OUD, are currently receiving OAT, and/or were previously receiving OAT and will compare opioid analgesics versus any comparators (including no treatment). For studies that enrolled a mixed population, the evidence synthesis team will include those that reported results for participants of interest separately or for at least 85% of the enrolled patients according to the eligibility criteria of our systematic review (refer to Table 1).

Case reports, case series, and conference abstracts will not be considered eligible. We will also exclude studies that enrolled patients presenting with acute pain (including acute postoperative pain), those with chronic pain related to cancer, those with end of life pain, and those receiving palliative or hospice care.

Data Extraction and Critical Appraisal

A data extraction form in Excel will be developed and the extraction criteria will be pilot tested. All reviewers will extract data from a subset of studies, and the evidence synthesis team will compare and review their data against the extractions of a subject matter expert. After reaching a consensus on the data extraction criteria, pairs of reviewers will independently extract data. The aim is to collect 5 groups of data: **study characteristics** (i.e., author, year, country, source of funding, and setting), **study methods** (i.e., study design, number of arms, primary objective, and research question), **participant information** (i.e., inclusion and exclusion criteria, age, sex, race and ethnicity, education level, underlying cause of chronic pain, study definition of OUD, information regarding current use of OAT, previous treatment with OAT, diagnosis of OUD, history of OUD, and coexisting psychiatric comorbidity), **interventions and comparison** (i.e., dose, duration and timing, formulation, route of administration, and comedication information), and **outcomes** (i.e., tools, scale of measurement, range, direction of outcome, and longest length of follow-up). The primary efficacy and effectiveness outcomes of interest are pain intensity, health-related quality of life, physical functioning, emotional functioning, and global rating of improvement. The primary safety outcomes are relapse, misuse, abuse, diversion, overdose, hospitalization, and death. All conflicts regarding data extraction will be resolved through discussion and, if needed, with the involvement of a senior reviewer.

Quality Assessment

We will assess risk of bias as part of data extraction by the same pairs of reviewers independently using the Cochrane risk-of-bias tool (RoB 2) for RCTs, which covers 5 domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcomes data (> 20% missing data will be considered a high risk of bias), bias in the measurement of the outcome, and reporting bias.[47]

We will also use the ROBINS-I tool for assessing risk of bias in nonrandomized studies. This tool covers 7 domains: bias due to confounding, bias in the selection of participants into the study, bias in classification of interventions, and bias due to deviations from the intended interventions, bias due to missing data, bias in the measurement of the outcome, and bias in selection of the reported result.[48]

Data Analysis and Synthesis

For both research questions, the evidence synthesis team will narratively summarize and report effect estimates. Whenever possible, all continuous outcome measures that are reported as the mean difference and the associated 95% CI will be reported. For binary outcomes, the evidence synthesis team will aim to report baseline probability for the outcome, a measure of association (e.g., relative risk, OR, hazard ratio), and a corresponding 95% CI. The evidence synthesis team will aim to narratively synthesize findings across study types and outcome types. A quantitative meta-synthesis will not be conducted for any outcomes.

Opportunities for Stakeholder Feedback

Stakeholders, including health care professionals, patients, drug manufacturers, and/or relevant associations will be given the opportunity to comment on the protocol, as well as to provide feedback on the draft report. Data identified as part of the feedback process may only be included if the source of data is in the public domain and fulfills the aforementioned selection criteria.

Areas for Potential Amendments

If amendments are required at any time during the study, the reasons for the changes will be recorded in a study file and subsequently reported within the final study report. If necessary, a rescreening of the previous literature search or an updated literature search will be performed to capture additional data according to the amendments.

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Appendix 1: Literature Search Strategy

Note that this appendix has not been copy-edited.

Database: Medline

1. (chronic adj4 pain*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (76319)
2. Chronic Pain/ (16300)
3. exp Osteoarthritis/ (66436)
4. osteoarthrit*.mp. (96448)
5. osteo-arthritis.mp. (391)
6. degenerative arthrit*.mp. (1339)
7. exp Arthritis, Rheumatoid/ (115736)
8. exp Neuralgia/ (21418)
9. Diabetic Neuropathies/ (15017)
10. (neuropath* adj5 (pain* or diabet*)).mp. (45703)
11. neuralg*.mp. (29057)
12. zoster.mp. (21893)
13. Irritable Bowel Syndrome/ (7744)
14. (IBS or irritable colon or irritable bowel).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (17682)
15. Migraine Disorders/ (26132)
16. migraine.mp. (40639)
17. Fibromyalgia/ (8738)
18. fibromyalg*.mp. (12427)
19. complex regional pain syndromes/ or exp causalgia/ or exp reflex sympathetic dystrophy/ (5637)
20. (complex regional pain syndromes or causalgia).mp. (2536)
21. Pain, Intractable/ (6238)
22. Phantom Limb/ (1922)
23. Hyperalgesia/ (12280)

24. ((noncancer* or non-cancer*or chronic* or recurrent or persist* or non-malign*) adj3 pain).mp. (20349)
25. or/1-24 (447084)
26. exp back pain/ or exp failed back surgery syndrome/ or exp low back pain/ (40359)
27. Radiculopathy/ or radiculopathy.mp. (9652)
28. musculoskeletal pain/ or headache/ (32001)
29. exp Arthralgia/ (13915)
30. exp Headache Disorders/ (35578)
31. headache*.mp. (98990)
32. Temporomandibular Joint Dysfunction Syndrome/ (4910)
33. ((TMJ or TMJD) and pain*).mp. (2931)
34. whiplash.mp. or exp whiplash injury/ (4054)
35. exp Cumulative Trauma Disorders/ (14071)
36. exp Peripheral Nervous System Diseases/dt [Drug Therapy] (15402)
37. Pain Measurement/de [Drug Effects] (6801)
38. (backache* or backpain* or dorsalgi* or arthralgi* or polyarthralgi* or arthrodyni* or myalgi* or fibromyalgi* or myodyni* or neuralgi* or ischialgi* or crps or rachialgi*).ab,ti. (48176)
39. ((back or discogen* or bone or musculoskelet* or muscle* or skelet* or spinal or spine or vertebra* or joint* or arthritis or Intestin* or neuropath* or neck or cervical* or head or facial* or complex or radicular or cervicobrachi* or orofacial or somatic or shoulder* or knee* or hip or hips) adj3 pain).mp. (180190)
40. ((medication* or opioid* or opiate* or narcotic*) and pain).mp. (88068)
41. or/26-40 (427849)
42. (acute or emergency or preoperative or postoperative).ti,ab. (2068161)
43. 41 not 42 (345619) (Excluding acute pain)
44. 25 or 43 (666455) (Chronic pain (total))
45. exp Analgesics, Opioid/ (120400)
46. (opioid* or opiate*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (141323)
47. (alfentanil or alphaprodine or beta-casomorphin$ or buprenorphine or carfentanil or codeine or deltorphin or dextromethorphan or dezocine or dihydrocodeine or dihydromorphine or enkephalin$ or ethylketocyclazocine or ethylmorphine or etorphine or fentanyl or heroin or hydrocodone or hydromorphone or ketobemidone or levorphanol or lofentanil or meperidine or

meptazinol or methadone or methadyl acetate or morphine or nalbuphine or opium or oxycodone or oxymorphone or pentazocine or phenazocine or phenoperidine or pirinitramide or promedol or propoxyphene or remifentanil or sufentanil or tilidine or tapentadol).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (159909)

48. or/45-47 (232170)
49. exp Narcotics/ (128525)
50. narcotic*.mp. (62757)
51. (adolonta or Anpec or Ardinex or Asimadoline or Alvimopam or amadol or biodalgic or biokanol or Codinovo or contramal or Demerol or Dicodid or Dihydrocodeinone or dihydromorphinone or dihydrohydroxycodeinone or dihydrone or dilaudid or dinarkon or dolsin or dolosal or dolin or dolantin or dolargan or dolcontral or duramorph or duromorph or duragesic or durogesic or eucodal or Fedotzine or Fentanest or Fentora or Fortral or Hycodan or Hycon or Hydrocodone or Hydrocodeinonebitartrate or hydromorphon or hydroxycodeinon or isocodeine or isonipecain or jutadol or laudacon or l dromoran or levodroman or levorphan or levo-dromoran or levodromoran or lexir or lidol or lydol or morfin or morfine or morphia or morphin or morphinium or morphinene or morphium or ms contin or n-methylmorphine or n methylmorphine or nobligan or numorphan or oramorph or oxycodeinon or oxiconum or oxycone or oxycontin or palladone or pancodine or pethidine or phentanyl or prontofort or robidone or skenan or sublimaze or sulfentanyl or sulfentanil or sufenta or takadol or talwin or theocodin or tramadol or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or tramundin or trasedal or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or tramadorsch or tramadin or tramadoc or ultram or zamudol or zumalgic or zydol or zytram).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (11346)
52. or/45-51 (263279)
53. exp Prescription Drug Misuse/ (14308)
54. exp opioid-related disorders/ (28351)
55. "Drug and Narcotic Control"/ (8870)
56. substance abuse detection/ (9661)
57. Drug Utilization/sn (6668)
58. Inappropriate Prescribing/sn (1437)
59. or/53-58
60. Drug-Seeking Behavior/ (1426)
61. Behavior, Addictive/ (10556)

62. Substance Withdrawal Syndrome/ (21635)
63. Poisoning/ (22498)
64. "Drug-Related Side Effects and Adverse Reactions"/ (33499)
65. accidents/ or accidental falls/ or accidents, traffic/ (85369)
66. substance-related disorders/ (97656)
67. Opioid-Related Disorders/ (16439)
68. or/ 60-67
69. (Opioid* or opiate* or narcotic* or analges* or prescription*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (407327)
70. 68 and 69 (SUD limit to opioid)
72. ((Opioid* or opiate* or narcotic* or analges* or prescription*) adj3 (abuse or addict* or misuse or overdose or poison* or diversion or aberrant or monitoring or mortality or death or suicide or coroner or (prob* adj2 "drug use"))).mp. (18172)
73. (behav* adj3 (nonmedical or nontherapeutic or abberant)).mp. (30)
74. 59 or 70 or 72 or73 (Total SUD & OUD)
75. (systematic review or meta-analysis).pt. (316513)
76. meta-analysis/ or systematic review/ or systematic reviews as topic/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/ or network meta-analysis/ (354883)
77. ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf. (322785)
78. ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf. (15730)
79. ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf. (39038)
80. (data synthes* or data extraction* or data abstraction*).ti,ab,kf. (40704)
81. (handsearch* or hand search*).ti,ab,kf. (11169)
82. (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf. (35833)
83. (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf. (12195)
84. (meta regression* or metaregression*).ti,ab,kf. (14653)

85. (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw. (470110)
86. (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw. (343797)
87. (cochrane or (health adj2 technology assessment) or evidence report).jw. (21497)
88. (comparative adj3 (efficacy or effectiveness)).ti,ab,kf. (17617)
89. (outcomes research or relative effectiveness).ti,ab,kf. (11256)
90. ((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf. (4342)
91. [(meta-analysis or systematic review).md.] (0)
92. (multi* adj3 treatment adj3 comparison*).ti,ab,kf. (295)
93. (mixed adj3 treatment adj3 (meta-analy* or metaanaly*)).ti,ab,kf. (179)
94. umbrella review*.ti,ab,kf. (1519)
95. (multi* adj2 paramet* adj2 evidence adj2 synthesis).ti,ab,kf. (14)
96. (multiparamet* adj2 evidence adj2 synthesis).ti,ab,kf. (18)
97. (multi-paramet* adj2 evidence adj2 synthesis).ti,ab,kf. (12)
98. or/75-97
99. exp clinical pathway/ (7805)
100. exp clinical protocol/ (190093)
101. clinical protocols/ (29902)
102. exp consensus/ (20898)
103. exp consensus development conference/ (12660)
104. exp consensus development conferences as topic/ (3000)
105. critical pathways/ (7805)
106. exp guideline/ (37781)
107. guidelines as topic/ (42069)
108. exp practice guideline/ (30519)
109. practice guidelines as topic/ (127541)
110. health planning guidelines/ (4165)
111. exp treatment guidelines/ (0)
112. Clinical Decision Rules/ (921)
113. (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt. (47682)

114. (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf. (46552)
115. (standards or guideline or guidelines).ti,kf. (136133)
116. ((practice or treatment* or clinical) adj guideline*).ab. (53112)
117. (CPG or CPGs).ti. (6449)
118. consensus*.ti,kf. (35112)
119. consensus*.ab. /freq=2 (34429)
120. ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf. (26765)
121. recommendat*.ti,kf. or guideline recommendation*.ab. (58820)
122. (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf. (84255)
123. (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf. (10236)
124. (algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kf. (12928)
125. (guideline* or standards or consensus* or recommendat*).au. (10)
126. [(guideline* or standards or consensus* or recommendat*).co.] (0)
127. (guideline* or standards or consensus* or recommendat*).ca. (1612)
128. or/99-127
129. Epidemiologic Methods/ (31616)
130. exp Epidemiologic Studies/ (3149024)
131. Observational Studies as Topic/ (8885)
132. Clinical Studies as Topic/ (789)
133. single-case studies as topic/ (98)
134. (Observational Study or Validation Studies or Clinical Study).pt. (149473)
135. (observational adj3 (study or studies or design or analysis or analyses)).ti,ab,kf. (221753)
136. cohort*.ti,ab,kf. (863693)
137. (prospective adj7 (study or studies or design or analysis or analyses)).ti,ab,kf. (535035)
138. ((follow up or followup) adj7 (study or studies or design or analysis or analyses)).ti,ab,kf. (170303)
139. ((longitudinal or longterm or (long adj term)) adj7 (study or studies or design or analysis or analyses or data)).ti,ab,kf. (347817)

140. (retrospective adj7 (study or studies or design or analysis or analyses or data or review)).ti,ab,kf. (685036)
141. ((case adj control) or (case adj comparison) or (case adj controlled)).ti,ab,kf. (159981)
142. (case-referent adj3 (study or studies or design or analysis or analyses)).ti,ab,kf. (638)
143. (population adj3 (study or studies or analysis or analyses)).ti,ab,kf. (234296)
144. (descriptive adj3 (study or studies or design or analysis or analyses)).ti,ab,kf. (110009)
145. ((multidimensional or (multi adj dimensional)) adj3 (study or studies or design or analysis or analyses)).ti,ab,kf. (4984)
146. (cross adj sectional adj7 (study or studies or design or research or analysis or analyses or survey or findings)).ti,ab,kf. (439128)
147. ((natural adj experiment) or (natural adj experiments)).ti,ab,kf. (3321)
148. (quasi adj (experiment or experiments or experimental)).ti,ab,kf. (20541)
149. ((non experiment or nonexperiment or non experimental or nonexperimental) adj3 (study or studies or design or analysis or analyses)).ti,ab,kf. (1719)
150. (prevalence adj3 (study or studies or analysis or analyses)).ti,ab,kf. (49797)
151. case series.ti,ab,kf. (103877)
152. case reports.pt. (2346603)
153. (case adj3 (report or reports or study or studies or histories)).ti,ab,kf. (983691)
154. organizational case studies/ (12631)
155. or/129-154
156. 98 or 124 or 155
156. 44 AND 52 AND 74 AND 156
157. animals/ not humans/ (4791092)
158. exp Animals, Laboratory/ (901737)
159. exp Animal Experimentation/ (9684)
160. exp Models, Animal/ (592322)
161. exp Rodentia/ (3309846)
162. (rat or rats or mouse or mice).ti. (1363634)
163. or/157-162
164. 156 not 163

Database: Embase

1. (chronic adj4 pain*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (125002)
2. chronic pain/ (65194)
3. exp osteoarthritis/ (136551)
4. osteoarthrit*.mp. (153027)
5. osteo-arthritis.mp. (440)
6. degenerative arthrit*.mp. (1613)
7. exp rheumatoid arthritis/ (209398)
8. exp neuralgia/ (110015)
9. diabetic neuropathy/ (24878)
10. (neuropath* adj5 (pain* or diabet*)).mp. (80274)
11. neuralg*.mp. (31802)
12. zoster.mp. (40221)
13. irritable colon/ (27468)
14. (Irritable Bowel Syndrome or IBS).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (26916)
15. exp migraine/ (66654)
16. migraine.mp. (73757)
17. fibromyalgia/ (21472)
18. fibromyalg*.mp. (23329)
19. reflex sympathetic dystrophy.mp. (2367)
20. (complex regional pain syndromes or causalgia).mp. (1315)
21. intractable pain/ (5012)
22. phantom limb.mp. or agnosia/ or phantom pain/ or amputation stump/ (7866)
23. hyperalgesia/ (19693)
24. ((noncancer* or non-cancer*or chronic* or recurrent or persist* or non-malign*) adj3 pain).mp. (30190)
25. or/1-24 (775064)
26. exp backache/ (115864)

27. radiculopathy.mp. or exp radiculopathy/ (40963)
28. musculoskeletal pain/ (12033)
29. exp arthralgia/ (64906)
30. headache/ (226226)
31. headache*.mp. (292451)
32. temporomandibular joint disorder/ (14501)
33. ((TMJ or TMJD) and pain*).mp. (3994)
34. whiplash.mp. or whiplash injury/ (5059)
35. exp cumulative trauma disorder/ (21894)
36. ((medication* or opioid* or opiate* or narcotic*) and pain).mp. (154398)
37. or/26-36 (642738)
38. (acute or emergency or preoperative or postoperative).ti,ab. (2826723)
39. 37 not 38 (517733)
40. 25 or 39 (1146023)
41. exp narcotic analgesic agent/ (347645)
42. (opioid* or opiate*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (211666)
43. (alfentanil or alphaprodine or beta-casomorphin$ or buprenorphine or carfentanil or codeine or deltorphin or dextromethorphan or dezocine or dihydrocodeine or dihydromorphine or enkephalin$ or ethylketocyclazocine or ethylmorphine or etorphine or fentanyl or heroin or hydrocodone or hydromorphone or ketobemidone or levorphanol or lofentanil or meperidine or meptazinol or methadone or methadyl acetate or morphine or nalbuphine or opium or oxycodone or oxymorphone or pentazocine or phenazocine or phenoperidine or pirinitramide or promedol or propoxyphene or remifentanil or sufentanil or tilidine or tapentadol).mp. (298666)
44. (adolonta or Anpec or Ardinex or Asimadoline or Alvimopam or amadol or biodalgic or biokanol or Codinovo or contramal or Demerol or Dicodid or Dihydrocodeinone or dihydromorphinone or dihydrohydroxycodeinone or dihydrone or dilaudid or dinarkon or dolsin or dolosal or dolin or dolantin or dolargan or dolcontral or duramorph or duromorph or duragesic or durogesic or eucodal or Fedotzine or Fentanest or Fentora or Fortral or Hycodan or Hycon or Hydrocodone or Hydrocodeinonebitartrate or hydromorphon or hydroxycodeinon or isocodeine or isonipecain or jutadol or laudacon or l dromoran or levodroman or levorphan or levo-dromoran or levodromoran or lexir or lidol or lydol or morfin or morfine or morphia or morphin or morphinium or morphinene or morphium or ms contin or n-methylmorphine or n methylmorphine or nobligan or numorphan or oramorph or oxycodeinon or oxiconum or oxycone or oxycontin or palladone or pancodine or pethidine or phentanyl or prontofort or robidone or skenan or sublimaze or sulfentanyl or sulfentanil or sufenta or takadol or talwin or theocodin or tramadol or tramadolhameln or

tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or tramundin or trasedal or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or tramadorsch or tramadin or tramadoc or ultram or zamudol or zumalgic or zydol or zytram).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (54623)

45. or/41-44 (440589)
46. opiate addiction/ (22619)
47. narcotic dependence/ or morphine addiction/ (4331)
48. prescription drug diversion/ (370)
49. or/46-48
50. drug abuse/ or analgesic agent abuse/ or drug misuse/ (61308)
51. drug control/ (11726)
52. drug monitoring/ (54894)
53. substance abuse/ (54984)
54. drug urine level/ (32300)
55. drug dose regimen/ (35206)
56. drug overdose/ (30250)
57. drug seeking behavior/ (2717)
58. drug dependence/ (58023)
59. addiction/ (48322)
60. drug withdrawal/ (210460)
61. withdrawal syndrome/ (29140)
62. intoxication/ (179248)
63. accident/ or falling/ or home accident/ or traffic accident/ (126306)
64. suicide/ or suicidal behavior/ or suicide attempt/ (93381)
65. or/50-64
66. (Opioid* or opiate* or narcotic* or analges* or prescription*).ti,ab. (464941)
67. 65 and 69
68. ((Opioid* or opiate* or narcotic* or analges* or prescription*) adj3 (abuse or addict* or misuse or overdose or poison* or diversion or aberrant or monitoring or mortality or death or suicide or coroner or (prob* adj2 "drug use"))).mp. (40929)
69. 49 or 67 or 68

70. observational study/
71. cohort analysis/
72. longitudinal study/
73. follow up/
74. retrospective study/
75. exp case control study/
76. cross-sectional study/
77. quasi experimental study/
78. prospective study/
79. (observational adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.
80. cohort*.ti,ab,kf.
81. (prospective adj7 (study or studies or design or analysis or analyses)).ti,ab,kf.
82. ((follow up or followup) adj7 (study or studies or design or analysis or analyses)).ti,ab,kf.
83. ((longitudinal or longterm or (long adj term)) adj7 (study or studies or design or analysis or analyses or data)).ti,ab,kf.
84. (retrospective adj7 (study or studies or design or analysis or analyses or data or review)).ti,ab,kf.
85. ((case adj control) or (case adj comparison) or (case adj controlled)).ti,ab,kf.
86. (case-referent adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.
87. (population adj3 (study or studies or analysis or analyses)).ti,ab,kf.
88. (descriptive adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.
89. ((multidimensional or (multi adj dimensional)) adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.
90. (cross adj sectional adj7 (study or studies or design or research or analysis or analyses or survey or findings)).ti,ab,kf.
91. ((natural adj experiment) or (natural adj experiments)).ti,ab,kf.
92. (quasi adj (experiment or experiments or experimental)).ti,ab,kf.
93. ((non experiment or nonexperiment or non experimental or nonexperimental) adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.
94. (prevalence adj3 (study or studies or analysis or analyses)).ti,ab,kf.
95. case series.ti,ab,kf.
96. case study/
97. case report/
98. (case adj3 (report or reports or study or studies or histories)).ti,ab,kf.

99. or/70-98
100. (systematic review or meta-analysis).pt.
101. meta-analysis/ or systematic review/ or systematic reviews as topic/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/ or network meta-analysis/
102. ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf.
103. ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf.
104. ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf.
105. (data synthes* or data extraction* or data abstraction*).ti,ab,kf.
106. (handsearch* or hand search*).ti,ab,kf.
107. (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf.
108. (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf.
109. (meta regression* or metaregression*).ti,ab,kf.
110. (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
111. (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.
112. (cochrane or (health adj2 technology assessment) or evidence report).jw.
113. (comparative adj3 (efficacy or effectiveness)).ti,ab,kf.
114. (outcomes research or relative effectiveness).ti,ab,kf.
115. ((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf.
116. (meta-analysis or systematic review).md.
117. (multi* adj3 treatment adj3 comparison*).ti,ab,kf.
118. (mixed adj3 treatment adj3 (meta-analy* or metaanaly*)).ti,ab,kf.
119. umbrella review*.ti,ab,kf.
120. (multi* adj2 paramet* adj2 evidence adj2 synthesis).ti,ab,kf.
121. (multiparamet* adj2 evidence adj2 synthesis).ti,ab,kf.
122. (multi-paramet* adj2 evidence adj2 synthesis).ti,ab,kf.
123. or/100-122
124. exp clinical pathway/

125. exp clinical protocol/
126. clinical protocols/
127. exp consensus/
128. exp consensus development conference/
129. exp consensus development conferences as topic/
130. critical pathways/
131. exp guideline/
132. guidelines as topic/
133. exp practice guideline/
134. practice guidelines as topic/
135. health planning guidelines/
136. exp treatment guidelines/
137. Clinical Decision Rules/
138. (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.
139. (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf.
140. (standards or guideline or guidelines).ti,kf.
141. ((practice or treatment* or clinical) adj guideline*).ab.
142. (CPG or CPGs).ti.
143. consensus*.ti,kf.
144. consensus*.ab. /freq=2
145. ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf.
146. recommendat*.ti,kf. or guideline recommendation*.ab.
147. (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf.
148. (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf.
149. (algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kf.
150. (guideline* or standards or consensus* or recommendat*).au.
151. (guideline* or standards or consensus* or recommendat*).co.
152. (guideline* or standards or consensus* or recommendat*).ca.
153. or/124-153

154. 99 or 123 or 153
155. 40 AND 45 AND 69 AND 154
156. exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/ (28918360)
157. human/ or normal human/ or human cell/ (22322879)
160. animals/ not humans/ (983946)
161. nonhuman/ (6525527)
162. exp Animal Experiment/ (2687886)
163. exp Experimental Animal/ (714449)
164. exp Rodent/ (3671555)
165. (rat or rats or mouse or mice).ti. (1502232)
166. or/ 156-165 (Non-Human concept)
167. 155 NOT 166 (Final results)

Database: PsycINFO

1. (chronic adj4 pain*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (23905)
2. chronic pain/ (14179)
3. exp arthritis/ (4366)
4. osteoarthrit*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (2287)
5. osteo-arthritis.mp. (8)
6. degenerative arthrit*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (15)
7. exp neuralgia/ (973)
8. exp neuropathy/ (6475)
9. (neuropath* adj5 (pain* or diabet*)).mp. (7288)
10. neuralg*.mp. (3464)
11. zoster.mp. (598)
12. irritable bowel syndrome/ (1210)
13. (IBS or irritable colon or irritable bowel).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (2108)
14. migraine headache/ (9426)

15. migraine.mp. (12623)
16. fibromyalgia/ (2112)
17. fibromyalg*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (3615)
18. complex regional pain syndromes.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (323)
19. "complex regional pain syndrome (type i)"/ (174)
20. (complex regional pain syndromes or causalgia).mp. (413)
21. somatosensory disorders/ (1493)
22. hyperalgesi*.mp. (5579)
23. somatoform pain disorder/ (850)
24. somatoform disorders/ (7886)
25. conversion disorder/ (1075)
26. ((noncancer* or non-cancer*or chronic* or recurrent or persist* or non-malign*) adj3 pain).mp. (3566)
27. or/1-26 (67174)
28. back pain.mp. or exp Back Pain/ (6448)
29. radiculopathy.mp. (348)
30. musculoskeletal pain.mp. (1912)
31. Arthralgia.mp. (337)
32. headache.mp. or exp HEADACHE/ (21143)
33. ((TMJ or TMJD) and pain*).mp. (158)
34. WHIPLASH/ or whiplash.mp. (616)
35. (backache* or backpain* or dorsalgi* or arthralgi* or polyarthralgi* or arthrodyni* or myalgi* or fibromyalgi* or myodyni* or neuralgi* or ischialgi* or crps or rachialgi*).ab,ti. (6240)
36. ((back or discogen* or bone or musculoskelet* or muscle* or skelet* or spinal or spine or vertebra* or joint* or arthritis or Intestin* or neuropath* or neck or cervical* or head or facial* or complex or radicular or cervicobrachi* or orofacial or somatic or shoulder* or knee* or hip or hips) adj3 pain).mp. (22027)
37. ((medication* or opioid* or opiate* or narcotic*) and pain).mp. (15283)
38. or/28-37 (57700)
39. (acute or emergency or preoperative or postoperative).ti,ab. (128922)
40. 38 not 39 (50357)

41. 27 or 40 (88522)
42. exp opiates/ (27037)
43. (opioid* or opiate*).mp. (35096)
44. (alfentanil or alphaprodine or beta-casomorphin$ or buprenorphine or carfentanil or codeine or deltorphin or dextromethorphan or dezocine or dihydrocodeine or dihydromorphine or enkephalin$ or ethylketocyclazocine or ethylmorphine or etorphine or fentanyl or heroin or hydrocodone or hydromorphone or ketobemidone or levorphanol or lofentanil or meperidine or meptazinol or methadone or methadyl acetate or morphine or nalbuphine or opium or oxycodone or oxymorphone or pentazocine or phenazocine or phenoperidine or pirinitramide or promedol or propoxyphene or remifentanil or sufentanil or tilidine or tapentadol).mp. (32725)
45. exp narcotic drugs/ (31229)
46. narcotic*.mp. (12271)
47. (adolonta or Anpec or Ardinex or Asimadoline or Alvimopam or amadol or biodalgic or biokanol or Codinovo or contramal or Demerol or Dicodid or Dihydrocodeinone or dihydromorphinone or dihydrohydroxycodeinone or dihydrone or dilaudid or dinarkon or dolsin or dolosal or dolin or dolantin or dolargan or dolcontral or duramorph or duromorph or duragesic or durogesic or eucodal or Fedotzine or Fentanest or Fentora or Fortral or Hycodan or Hycon or Hydrocodone or Hydrocodeinonebitartrate or hydromorphon or hydroxycodeinon or isocodeine or isonipecain or jutadol or laudacon or l dromoran or levodroman or levorphan or levo-dromoran or levodromoran or lexir or lidol or lydol or morfin or morfine or morphia or morphin or morphinium or morphinene or morphium or ms contin or n-methylmorphine or n methylmorphine or nobligan or numorphan or oramorph or oxycodeinon or oxiconum or oxycone or oxycontin or palladone or pancodine or pethidine or phentanyl or prontofort or robidone or skenan or sublimaze or sulfentanyl or sulfentanil or sufenta or takadol or talwin or theocodin or tramadol or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or tramundin or trasedal or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or tramadorsch or tramadin or tramadoc or ultram or zamudol or zumalgic or zydol or zytram).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (1124)
48. or/42-47 (57076)
49. drug dependency/ (12925)
50. drug abuse/ (47752)
51. drug rehabilitation/ (21752)
52. "substance use disorder"/ (8448)
53. self-medication/ (718)
54. prescription drugs/ (5147)
55. drug overdoses/ (2091)
56. exp drug addiction/ (19576)

57. drug seeking/ (1063)
58. addiction/ (11648)
59. drug withdrawal/ (5960)
60. toxic disorders/ (1561)
61. "side effects (drug)"/ (26415)
62. drug tolerance/ (4601)
63. exp accidents/ (14353)
64. exp "death and dying"/ (41493)
65. suicide/ or self-destructive behavior/ or attempted suicide/ or self-injurious behavior/ or suicidal ideation/ or suicide prevention/ (47617)
67. or/49-65
68. (Opioid* or opiate* or narcotic* or analges* or prescription*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (72778)
69. 67 AND 68
70. ((Opioid* or opiate* or narcotic* or analges* or prescription*) adj3 (abuse or addict* or misuse or overdose or poison* or diversion or aberrant or monitoring or mortality or death or suicide or coroner or (prob* adj2 "drug use"))).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (8489)
71. 69 OR 71
72. cohort analysis/ (1699)
73. longitudinal studies/ (16107)
74. prospective studies/ (1312)
75. retrospective studies/ (934)
76. followup studies/ (12397)
77. quasi experimental methods/ (506)
78. (observational adj3 (study or studies or design or analysis or analyses)).ti,ab. (18927)
79. cohort*.ti,ab. (97823)
80. (prospective adj7 (study or studies or design or analysis or analyses)).ti,ab. (46322)
81. ((follow up or followup) adj7 (study or studies or design or analysis or analyses)).ti,ab. (32999)
82. ((longitudinal or longterm or (long adj term)) adj7 (study or studies or design or analysis or analyses or data))
83. (retrospective adj7 (study or studies or design or analysis or analyses or data or review)).ti,ab. (31208)

84. ((case adj control) or (case adj comparison) or (case adj controlled)).ti,ab. (13337)
85. (case-referent adj3 (study or studies or design or analysis or analyses)).ti,ab. (20)
86. (population adj3 (study or studies or analysis or analyses)).ti,ab. (33516)
87. (descriptive adj3 (study or studies or design or analysis or analyses)).ti,ab. (33476)
88. ((multidimensional or (multi adj dimensional)) adj3 (study or studies or design or analysis or analyses)).ti,ab.
89. (cross adj sectional adj7 (study or studies or design or research or analysis or analyses or survey or findings))
90. ((natural adj experiment) or (natural adj experiments)).ti,ab. (1570)
91. (quasi adj (experiment or experiments or experimental)).ti,ab. (15846)
92. ((non experiment or nonexperiment or non experimental or nonexperimental) adj3 (study or studies or design or ana
93. (prevalence adj3 (study or studies or analysis or analyses)).ti,ab. (9727)
94. case series.ti,ab. (4888)
95. (case adj3 (report or reports or study or studies or histories)).ti,ab. (168186)
96. case report/ (23364)
97. or/1-25 (621735)
98. (systematic review or meta-analysis).pt. (0)
99. meta-analysis/ or systematic review/ or systematic reviews as topic/ or meta-analysis as topic/ or "meta analysis
100. [((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf.] (0)
101. [((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf.]
102. [((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)
103. [(data synthes* or data extraction* or data abstraction*).ti,ab,kf.] (0)
104. [(handsearch* or hand search*).ti,ab,kf.] (0)
105. [(mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf.] (0)
106. [(met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisa
107. [(meta regression* or metaregression*).ti,ab,kf.] (0)

108. (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology a
109. (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw. (35940)
110. (cochrane or (health adj2 technology assessment) or evidence report).jw. (0)
111. [(comparative adj3 (efficacy or effectiveness)).ti,ab,kf.] (0)
112. [(outcomes research or relative effectiveness).ti,ab,kf.] (0)
113. [((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf.] (0)
114. (meta-analysis or systematic review).md. (64233)
115. [(multi* adj3 treatment adj3 comparison*).ti,ab,kf.] (0)
116. [(mixed adj3 treatment adj3 (meta-analy* or metaanaly*)).ti,ab,kf.] (0)
117. [umbrella review*.ti,ab,kf.] (0)
118. [(multi* adj2 paramet* adj2 evidence adj2 synthesis).ti,ab,kf.] (0)
119. [(multiparamet* adj2 evidence adj2 synthesis).ti,ab,kf.] (0)
120. [(multi-paramet* adj2 evidence adj2 synthesis).ti,ab,kf.] (0)
121. or/27-49 (104270)
122. exp clinical pathway/ (0)
123. exp clinical protocol/ (0)
124. clinical protocols/ (0)
125. exp consensus/ (0)
126. exp consensus development conference/ (0)
127. exp consensus development conferences as topic/ (0)
128. critical pathways/ (0)
129. exp guideline/ (0)
130. guidelines as topic/ (0)
131. exp practice guideline/ (0)
132. practice guidelines as topic/ (0)
133. health planning guidelines/ (0)
134. exp treatment guidelines/ (9284)
135. Clinical Decision Rules/ (0)
136. (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt
137. [(position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf.] (0)

138. [(standards or guideline or guidelines).ti,kf.] (0)
139. ((practice or treatment* or clinical) adj guideline*).ab. (9192)
140. (CPG or CPGs).ti. (140)
141. [consensus*.ti,kf.] (0)
142. consensus*.ab. /freq=2 (5795)
143. [((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf.] (0)
144. [recommendat*.ti,kf. or guideline recommendation*.ab.] (0)
145. [(care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf.] (0)
146. [(algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses
147. [(algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*))
148. (guideline* or standards or consensus* or recommendat*).au. (0)
149. (guideline* or standards or consensus* or recommendat*).co. (0)
150. (guideline* or standards or consensus* or recommendat*).ca. (299)
151. or/51-79 (21794)
152. 97 or 121 or 151
153. 41 AND 48 AND 71 AND 152

Database: CINAHL

#	Query
S75	S43 AND S51 AND S57 AND S74
S74	S72 AND S73
S73	Opioid* or opiate* or narcotic* or analges* or prescription*
S72	S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71
S71	(MH "Suicide+")
S70	(MH "Death+")
S69	(MH "Accidents") OR (MH "Accidental Falls") OR (MH "Accidents, Home") OR (MH "Accidents, Traffic")
S68	(MH "Adverse Drug Event+")

S67 (MH "Poisoning")

S66 (MH "Substance Withdrawal Syndrome")

S65 (MH "Behavior, Addictive")

S64 (MH "Substance Abuse Detection")

S63 (MH "Drug and Narcotic Control")

S62 (MH "Drug Toxicity")

S61 (MH "Overdose")

S60 (MH "Substance Use Disorders")

S59 (MH "Substance Dependence")

S58 (MH "Substance Abuse")

S57 S52 OR S53 OR S54 OR S55 OR S56

S56 (TI "case series" OR AB "case series") OR ((TI case OR AB case) N3 ((TI report OR AB report) OR (TI reports OR AB reports) OR (TI study OR AB study) OR (TI studies OR AB studies) OR (TI histories OR AB histories))) OR MH ("case studies")

S55 ((TI cross OR AB cross) W1 (TI sectional OR AB sectional) N7 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI research OR AB research) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses) OR (TI survey OR AB survey) OR (TI findings OR AB findings))) OR (((TI natural OR AB natural) W1 (TI experiment OR AB experiment)) OR ((TI natural OR AB natural) W1 (TI experiments OR AB experiments))) OR ((TI quasi OR AB quasi) W1 ((TI experiment OR AB experiment) OR (TI experiments OR AB experiments) OR (TI experimental OR AB experimental))) OR (((TI "non experiment" OR AB "non experiment") OR (TI nonexperiment OR AB nonexperiment) OR (TI "non experimental" OR AB "non experimental") OR (TI nonexperimental OR AB nonexperimental)) N3 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses))) OR ((TI prevalence OR AB prevalence) N3 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses)))

S54 MH "Nonexperimental Studies+") OR (MH "Correlational Studies") OR (MH "Control Group") OR (MH "Matched-Pair Analysis") OR ((TI observational OR AB observational) N3 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses))) OR (TI cohort* OR AB cohort*) OR ((TI prospective OR AB prospective) N7 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses))) OR (((TI "follow up" OR AB "follow up") OR (TI followup OR AB followup)) N7 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses))) OR (((TI longitudinal OR AB longitudinal) OR (TI longterm OR AB longterm) OR ((TI long OR AB long) W1 (TI term OR AB term))) N7 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI analysis OR AB analysis) OR (TI

analyses OR AB analyses) OR (TI data OR AB data))) OR ((TI retrospective OR AB retrospective) N7 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses) OR (TI data OR AB data) OR (TI review OR AB review))) OR (((TI case OR AB case) W1 (TI control OR AB control)) OR ((TI case OR AB case) W1 (TI comparison OR AB comparison)) OR ((TI case OR AB case) W1 (TI controlled OR AB controlled))) OR ((TI case-referent OR AB case-referent) N3 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses))) OR ((TI population OR AB population) N3 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses))) OR ((TI descriptive OR AB descriptive) N3 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses))) OR (((TI multidimensional OR AB multidimensional) OR ((TI multi OR AB multi) W1 (TI dimensional OR AB dimensional))) N3 ((TI study OR AB study) OR (TI studies OR AB studies) OR (TI design OR AB design) OR (TI analysis OR AB analysis) OR (TI analyses OR AB analyses)))

S53 MH Critical Path or MH Practice Guidelines or PT (practice guidelines or standards or protocol or critical path or care plan) or TI ("position statement*" or "policy statement*" or "practice parameter*" or "best practice*") OR AB ("position statement*" or "policy statement*" or "practice parameter*" or "best practice*") or TI (standards or guideline or guidelines) or AB (practice N1 guideline* or treatment* N1 guideline*) or TI (CPG or CPGs) or TI consensus* or AB consensus* or AU (guideline* or standards or consensus* or recommendat*) or CA (guideline* or standards or consensus* or recommendat*) or TI (critical N2 path or critical N2 paths or critical N2 pathway or critical N2 pathways or critical N2 protocol* or clinical N2 path or clinical N2 paths or clinical N2 pathway or clinical N2 pathways or clinical N2 protocol* or practice N2 path or practice N2 paths or practice N2 pathway or practice N2 pathways or practice N2 protocol*) or AB (critical N2 path or critical N2 paths or critical N2 pathway or critical N2 pathways or critical N2 protocol* or clinical N2 path or clinical N2 paths or clinical N2 pathway or clinical N2 pathways or clinical N2 protocol* or practice N2 path or practice N2 paths or practice N2 pathway or practice N2 pathways or practice N2 protocol*) or TI recommendat* or TI (care N2 path or care N2 paths or care N2 pathway or care N2 pathways or care N2 map or care N2 maps or care N2 plan or care N2 plans or care N2 standard*) or AB (care N2 path or care N2 paths or care N2 pathway or care N2 pathways or care N2 map or care N2 maps or care N2 plan or care N2 plans or care N2 standard*) or TI (algorithm* AND (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)) or AB (algorithm* AND (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)) or (PT algorithm* AND TI (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)) or (PT algorithm* AND AB (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)) or TI (algorithm* AND (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)) OR AB (algorithm* AND (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)) or (PT algorithm AND TI (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)) or (PT algorithm AND AB (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*))

S52 MH "meta analysis" OR MH "systematic review" OR MH "Technology, Medical/EV" OR PT "systematic review" OR PT "meta analysis" OR (((TI systematic* OR AB systematic*) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*))) OR ((TI methodologic* OR AB methodologic*) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*)))) OR (((TI quantitative OR AB quantitative) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*) OR (TI synthes* OR AB synthes*))) OR ((TI research OR AB research) N3 ((TI integrati* OR AB integrati*) OR (TI overview* OR AB overview*)))) OR (((TI integrative OR AB integrative) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*))) OR ((TI collaborative OR AB collaborative) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*))) OR ((TI pool* OR AB pool*) N3 (TI analy* OR AB analy*))) OR ((TI "data synthes*" OR AB "data synthes*") OR (TI "data extraction*" OR AB "data extraction*") OR (TI "data abstraction*" OR AB "data abstraction*")) OR ((TI handsearch* OR AB handsearch*) OR (TI "hand search*" OR AB "hand search*")) OR ((TI "mantel haenszel" OR AB "mantel haenszel") OR (TI peto OR AB peto) OR (TI "der simonian" OR AB "der simonian") OR (TI dersimonian OR AB dersimonian) OR (TI "fixed effect*" OR AB "fixed effect*") OR (TI "latin square*" OR AB "latin square*")) OR ((TI "met analy*" OR AB "met analy*") OR (TI metanaly* OR AB metanaly*) OR (TI "technology assessment*" OR AB "technology assessment*") OR (TI HTA OR AB HTA) OR (TI HTAs OR AB HTAs) OR (TI "technology overview*" OR AB "technology overview*") OR (TI "technology appraisal*" OR AB "technology appraisal*")) OR ((TI "meta regression*" OR AB "meta regression*") OR (TI metaregression* OR AB metaregression*)) OR (MW meta-analy* OR MW metaanaly* OR MW "systematic review*" OR MW "biomedical technology assessment*" OR MW "bio-medical technology assessment*") OR ((TI medline OR AB medline OR MW medline) OR (TI cochrane OR AB cochrane OR MW cochrane) OR (TI pubmed OR AB pubmed OR MW pubmed) OR (TI medlars OR AB medlars OR MW medlars) OR (TI embase OR AB embase OR MW embase) OR (TI cinahl OR AB cinahl OR MW cinahl)) OR (SO Cochrane OR SO health technology assessment OR SO evidence report) OR ((TI comparative OR AB comparative) N3 ((TI efficacy OR AB efficacy) OR (TI effectiveness OR AB effectiveness))) OR ((TI "outcomes research" OR AB "outcomes research") OR (TI "relative effectiveness" OR AB "relative effectiveness")) OR (((TI indirect OR AB indirect) OR (TI "indirect treatment" OR AB "indirect treatment") OR (TI mixed-treatment OR AB mixed-treatment) OR (TI bayesian OR AB bayesian)) N3 (TI comparison* OR AB comparison*)) OR ((TI multi* OR AB multi*) N3 (TI treatment OR AB treatment) N3 (TI comparison* OR AB comparison*)) OR ((TI mixed OR AB mixed) N3 (TI treatment OR AB treatment) N3 ((TI meta-analy* OR AB meta-analy*) OR (TI metaanaly* OR AB metaanaly*))) OR (TI "umbrella review*" OR AB "umbrella review*") OR ((TI multi* OR AB multi*) N2 (TI paramet* OR AB paramet*) N2 (TI evidence OR AB evidence) N2 (TI synthesis OR AB synthesis)) OR ((TI multiparamet* OR AB multiparamet*) N2 (TI evidence OR AB evidence) N2 (TI synthesis OR AB synthesis)) OR ((TI multi-paramet* OR AB multi-paramet*) N2 (TI evidence OR AB evidence) N2 (TI synthesis OR AB synthesis))

S51 S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50

S50 adolonta or Anpec or Ardinex or Asimadoline or Alvimopam or amadol or biodalgic or biokanol or Codinovo or contramal or Demerol or Dicodid or Dihydrocodeinone or dihydromorphinone or dihydrohydroxycodeinone or dihydrone or dilaudid or dinarkon or dolsin or dolosal or dolin or

dolantin or dolargan or dolcontral or duramorph or duromorph or duragesic or durogesic or eucodal or Fedotzine or Fentanest or Fentora or Fortral or Hycodan or Hycon or Hydrocodone or Hydrocodeinonebitartrate or hydromorphon or hydroxycodeinon or isocodeine or isonipecain or jutadol or laudacon or l dromoran or levodroman or levorphan or levo-dromoran or levodromoran or lexir or lidol or lydol or morfin or morfine or morphia or morphin or morphinium or morphinene or morphium or ms contin or n-methylmorphine or n methylmorphine or nobligan or numorphan or oramorph or oxycodeinon or oxiconum or oxycone or oxycontin or palladone or pancodine or pethidine or phentanyl or prontofort or robidone or skenan or sublimaze or sulfentanyl or sulfentanil or sufenta or takadol or talwin or theocodin or tramadol or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or tramundin or trasedal or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or tramadorsch or tramadin or tramadoc or ultram or zamudol or zumalgic or zydol or zytram

S49 alfentanil or alphaprodine or beta-casomorphin$ or buprenorphine or carfentanil or codeine or deltorphin or dextromethorphan or dezocine or dihydrocodeine or dihydromorphine or enkephalin$ or ethylketocyclazocine or ethylmorphine or etorphine or fentanyl or heroin or hydrocodone or hydromorphone or ketobemidone or levorphanol or lofentanil or meperidine or meptazinol or methadone or methadyl acetate or morphine or nalbuphine or opium or oxycodone or oxymorphone or pentazocine or phenazocine or phenoperidine or pirinitramide or promedol or propoxyphene or remifentanil or sufentanil or tilidine or tapentadol

S48 "narcotic*"

S47 (MH "Narcotics+")

S46 "opiate*"

S45 "opioid*"

S44 (MH "Analgesics, Opioid+")

S43 S26 OR S42

S42 S40 NOT S41

S41 acute or emergency or preoperative or postoperative

S40 S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39

S39 ((back or discogen* or bone or musculoskelet* or muscle* or skelet* or spinal or spine or vertebra* or joint* or arthritis or Intestin* or neuropath* or neck or cervical* or head or facial* or complex or radicular or cervicobrachi* or orofacial or somatic or shoulder* or knee* or hip or hips) N3 pain)

S38 backache* or backpain* or dorsalgi* or arthralgi* or polyarthralgi* or arthrodyni* or myalgi* or fibromyalgi* or myodyni* or neuralgi* or ischialgi* or crps or rachialgi*

S37 (MH "Peripheral Nervous System+/DE")

S36 (MH "Cumulative Trauma Disorders+")

S35 (MH "Whiplash Injuries") OR "whiplash"

S34 ((TMJ or TMJD) and pain*)

S33 (MH "Temporomandibular Joint Syndrome")

S32 "headache*"

S31 (MH "Headache")

S30 (MH "Arthralgia+")

S29 "musculoskeletal pain"

S28 (MH "Radiculopathy") OR "radiculopathy"

S27 (MH "Back Pain+")

S26 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25

S25 ((noncancer* or non-cancer*or chronic* or recurrent or persist* or non-malign*) N3 pain)

S24 (MH "Hyperalgesia")

S23 (MH "Phantom Limb") OR (MH "Phantom Pain")

S22 "intractable pain"

S21 "causalgia"

S20 (MH "Complex Regional Pain Syndromes+")

S19 "fibromyalg*"

S18 (MH "Fibromyalgia")

S17 "migraine"

S16 (MH "Migraine")

S15 "IBS"

S14 (irritable (bowel or colon))

S13 (MH "Irritable Bowel Syndrome")

S12 "zoster"

S11 "neuralg*"

S10 (neuropath* N5 (pain* or diabet*))

S9 (MH "Diabetic Neuropathies")

S8 (MH "Neuralgia+")

S7 (MH "Arthritis, Rheumatoid+")

S6 "degenerative arthrit*"

S5 "osteo-arthritis"

S4 "osteoarthrit*"

S3 (MH "Osteoarthritis+")

S2 chronic N4 pain

S1 (MH "Chronic Pain")

Database: AMED (Allied and Complementary Medicine) <1985 to August 2023>

Search Strategy

1. pain/ or abdominal pain/ or arthralgia/ or backache/ or facial pain/ or headache/ or musculoskeletal pain/ or neck pain/ or neuralgia/ or nociceptive pain/ or pain intractable/ (18826)
2. (chronic adj3 pain).mp. [mp=abstract, heading words, title] (5538)
3. osteo-arthritis.mp. (19)
4. degenerative arthrit*.mp. (53)
5. exp Arthritis rheumatoid/ or Arthritis, Rheumatoid.mp. (2297)
6. exp Osteoarthritis/ or osteoarthritis.mp. (4625)
7. exp Neuralgia/ or Neuralgia.mp. (474)
8. exp Diabetic neuropathies/ or Diabetic Neuropath$.mp. (1187)
9. (IBS or irritable colon or irritable bowel).mp. [mp=abstract, heading words, title] (403)
10. exp Migraine/ or migraine.mp. (827)
11. exp Fibromyalgia/ or Fibromyalgia.mp. (2000)
12. exp complex regional pain syndromes/ or complex regional pain syndromes.mp. (75)
13. exp Pain intractable/ or Pain, Intractable.mp. (464)
14. exp Phantom limb/ or Phantom Limb.mp. (191)
15. Hyperalgesia/ or Hyperalgesia.mp. (307)
16. ((noncancer* or non-cancer*or chronic* or recurrent or persist* or non-malign*) adj3 pain).mp. (888)
17. or/1-16 (31137)
18. exp back pain/ or exp failed back surgery syndrome/ or exp low back pain/ (5273)
19. Radiculopathy/ or radiculopathy.mp. (334)
20. musculoskeletal pain/ or headache/ (1393)

21. exp Arthralgia/ (260)
22. exp Headache/ or headache.mp. (2119)
23. exp Temporomandibular joint syndrome/ or Temporomandibular Joint Dysfunction Syndrome.mp. (76)
24. ((TMJ or TMJD) and pain*).mp. (89)
25. exp Whiplash injuries/ or whiplash.mp. (651)
26. exp repetition strain injury/ or cumulative trauma disorder/ (335)
27. cumulative trauma disorder.mp. (28)
28. exp Peripheral nervous system disease/ or Peripheral Nervous System Diseases.mp. (4234)
29. (backache* or backpain* or dorsalgi* or arthralgi* or polyarthralgi* or arthrodyni* or myalgi* or fibromyalgi* or myodyni* or neuralgi* or ischialgi* or crps or rachialgi*).ab,ti. (2759)
30. ((back or discogen* or bone or musculoskelet* or muscle* or skelet* or spinal or spine or vertebra* or joint* or arthritis or Intestin* or neuropath* or neck or cervical* or head or facial* or complex or radicular or cervicobrachi* or orofacial or somatic or shoulder* or knee* or hip or hips) adj3 pain).mp. (16120)
31. exp Pain measurement/ or Pain Measurement.mp. (2235)
32. 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 (25614)
33. (acute or emergency or preoperative or postoperative).ti,ab. (17441)
34. 32 not 33 (23523)
35. 17 or 34 (40752)
36. exp analgesics opioid/ or opioid.mp. or exp Narcotics/ or exp Morphine/ (1696)
37. (opioid* or opiate*).mp. [mp=abstract, heading words, title] (1867)
38. (alfentanil or alphaprodine or beta-casomorphin$ or buprenorphine or carfentanil or codeine or deltorphin or dextromethorphan or dezocine or dihydrocodeine or dihydromorphine or enkephalin$ or ethylketocyclazocine or ethylmorphine or etorphine or fentanyl or heroin or hydrocodone or hydromorphone or ketobemidone or levorphanol or lofentanil or meperidine or meptazinol or methadone or methadyl acetate or morphine or nalbuphine or opium or oxycodone or oxymorphone or pentazocine or phenazocine or phenoperidine or pirinitramide or promedol or propoxyphene or remifentanil or sufentanil or tilidine or tapentadol).mp. [mp=abstract, heading words, title] (1286)
39. narcotic$.mp. (380)
40. (adolonta or Anpec or Ardinex or Asimadoline or Alvimopam or amadol or biodalgic or biokanol or Codinovo or contramal or Demerol or Dicodid or Dihydrocodeinone or dihydromorphinone or

dihydrohydroxycodeinone or dihydrone or dilaudid or dinarkon or dolsin or dolosal or dolin or dolantin or dolargan or dolcontral or duramorph or duromorph or duragesic or durogesic or eucodal or Fedotzine or Fentanest or Fentora or Fortral or Hycodan or Hycon or Hydrocodone or Hydrocodeinonebitartrate or hydromorphon or hydroxycodeinon or isocodeine or isonipecain or jutadol or laudacon or l dromoran or levodroman or levorphan or levo-dromoran or levodromoran or lexir or lidol or lydol or morfin or morfine or morphia or morphin or morphinium or morphinene or morphium or ms contin or n-methylmorphine or n methylmorphine or nobligan or numorphan or oramorph or oxycodeinon or oxiconum or oxycone or oxycontin or palladone or pancodine or pethidine or phentanyl or prontofort or robidone or skenan or sublimaze or sulfentanyl or sulfentanil or sufenta or takadol or talwin or theocodin or tramadol or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or tramundin or trasedal or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or tramadorsch or tramadin or tramadoc or ultram or zamudol or zumalgic or zydol or zytram).mp. [mp=abstract, heading words, title] (140)

41. 36 or 37 or 38 or 39 or 40 (2786)
42. exp substance related disorders/ (1716)
43. (opioid* adj4 disorder*).mp. [mp=abstract, heading words, title] (50)
44. (Opioid* adj3 Abuse).mp. [mp=abstract, heading words, title] (31)
45. (Opioid* adj3 Dependence).mp. [mp=abstract, heading words, title] (22)
46. (opioid* adj3 addiction).mp. [mp=abstract, heading words, title] (45)
47. Opioid-Related Disorders.mp. (26)
48. (problematic adj3 opioid).mp. [mp=abstract, heading words, title] (3)
49. exp Buprenorphine/ or buprenorphine.mp. (58)
50. exp Methadone/ or methadone.mp. (155)
51. (opioid adj5 OAT).mp. [mp=abstract, heading words, title] (2)
52. opioid agonist treatment.mp. (1)
53. opioid agonist therapy.mp. (1)
54. 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 (1909)
55. 35 and 41 and 54 (203)

Appendix 2: Content and Methodological Experts

Note that this appendix has not been copy-edited.

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